REMARKS

Reconsideration is requested.

Claims 1-10, 12, 22 and 23 have been canceled, without prejudice.

Claim 11 has been revised to include the details of claim 12, without prejudice, to advance prosecution. The claims have been revised to define methods pf treatment, to advance prosecution. Claims 24-26 have been revised to define methods, dependent from claim 11. No new matter has been added. The claims are submitted to advance prosecution by at least reducing the issues for appeal, as further detailed below. The amendments are not believed to raise new issues requiring further search and/or consideration. No new matter has been added. Entry of the present Amendment is requested.

The Section 112, second paragraph, rejection of claim 11 is obviated by the above amendments. The objected-to term has been defined in the amended claim 11 by the terms added from dependent claim 12, which was not similarly rejected. Entry of the present Amendment will at least reduce the issue of the Section 112, second paragraph, rejection of claim 11 for appeal. Entry of the present Amendment and withdrawal of the Section 112, second paragraph, rejection of claim 11 are requested.

The Section 112, fourth paragraph, rejection of claims 22 and 23 will be moot upon the entry of the present Amendment. Entry of the present Amendment will at least reduce the issue of the Section 112, fourth paragraph, rejection of claims 22 and 23 for appeal. Entry of the present Amendment and withdrawal of the Section 112, fourth paragraph, rejection of claims 22 and 23 are requested.

The Section 103 rejection of claims 11-26 over Van Loo (Critical Reviews in Food Science and Nutrition, 35(6), 525-552 (1995)) in view of Beers (Chapter 5 ("Nutritional Disorders") in The Merck Manual of Diagnosis and Therapy, 17th Edition, Merck & Co., Inc., Rahway, NJ, 1999, only the pages and the text pages 58-62) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Initially, the applicants note the Examiner's mischaracterization that the claims are "directed to mixtures of fructose and fructooligosaccharides (FOS)" (see page 4 of the Office Action dated November 30, 2007) as opposed to the claims providing a method of treatment involving, in one embodiment, administration of FOS.

The Examiner will appreciate that fructose is a monosaccharide or a sugar. The applicants believe that a diet rich in sugars, such as fructose, leads to oxidative stress, which can be treated by the presently claimed invention. Specifically, the claimed invention describes treating oxidative stress, linked to the over consumption of sugars such as fructose, comprising the administration of food preparations, functional foods, or pharmaceutical compositions containing prebiotics which are at least one oligosaccharide chosen from: fructans, fructooligosaceharides (FOS), galactooligosaccharides, xylooligosaccharides, soybean oligosaccharides, gentiooligosaccharides, and isomaltooligosaccharides.

Although Van Loo and Beers may disclose the beneficial effect of oligosaccharides for health and recommend to replace lower sugars by complex one in case of diabetes or obesity, neither of the cited documents teach or suggest that

addition of complex sugars to lower sugars could be useful for treating oxidative stress due to said lower sugars.

Van Loo is understood to only deal with the nutritional properties of FOS and Beers is understood to relate to limitation of the caloric intake to decrease obesity.

In Van Loo, table 1 discloses the integrated values of the Gas chromatographic analysis of native chicory inulin, (extracted from freshly harvested roots), commercially available chicory inulin (Raftiline ®) and partial chicory inulin hydrolysate ((Raftilose ®) which contains 85% of oligofructoses and 15 % of lower sugar without describing what kind of oligofructose is used. Tables 6 and 10 of the reference are understood to disclose the contents of inulin respectively in Jerusalem Artichoke and garlic which are not food compositions but food stuffs, whereas table 9 teaches that food processing like roasting and cooking can be used to modify the contents of Inulin and oligofructose of foodstuffs. The applicants believe that none of these data suggest the specific compositions of the presently claimed invention, such as is recited in claims 24-26.

Although oxidative stress, obesity or high blood pressure are all consequences of over consumption of sugars like fructose, the applicants believe that the mechanism leading to such symptoms are completely different. Specifically, the applicants believe that oxidative stress is linked to the formation of free radicals which are responsible of an acceleration of ageing whereas obesity is due to an accumulation of adipose cells and hypertension to high sugar concentration in blood.

Even if the reduction of consumption of sugars was known to avoid obesity and diabetes, it would not have been obvious to a person of ordinary skill in the art at the time the invention was made that the reduction could have an anti ageing effect.

As for the Examiner's comments regarding guidance provided in the specification (see pages 5-6 of the Office Action dated November 30, 2007), the Examiner is requested to see the examples of the specification wherein the following four (4) groups of rats were studied: one group (A) fed with starch only, one group (F) fed with fructose only, one group (A/FOS) fed with starch and FOS, and one group (F/FOS) fed with fructose and FOS.

As described in the specification, measurements of the plasma levels of thiobarbituric acid (TBARS) allows evaluation of the oxidative stress, as the greater its value the greater the level of oxidative stress. The results are represented in the following Table:

	Group A	Group F	Group A/FOS	Group F/FOS
Plasma TBARS (nmol/ml)	1.94±0.03	2.14±0.07	1.84±0.02	1.96±0.04

The levels of plasma TBARS are significantly greater in Group F (+10% compared to Group A), confirming that fructose increases oxidative stress. The above further confirms that FOS has no effect on the starch regimen (Group A/FOS same level of TBARS as in Group A) whereas in the Group F/FOS the levels of TBARS are significantly decreased as compared to the Group F (-8%) and return the level to that of Group A. These results, which are presented and described in the present specification, show that inclusion of FOS avoids the increase of TBARS and treat the

oxidative stress due to fructose. Similar results were found with the urine and heart TBARS levels. These results of the specification are believed to demonstrate the unexpected benefit of the claimed invention.

Attached, for completeness are copies of abstracts of the following references relating to administration of Raftilose (FOS (see the Table on page 6 of the present application)):

Kok, N et al, Br. J. Nutr., 1996 Dec 76(6), 881-90 "Involvement of lipogenesis in the lower VLDL secretion induced by oligofructose in rats" (which is understood to describe that the administration of 100 g of Raftilose as oligofructose source for 30 days decreases *de novo* fatty acid synthesis in the liver leading to a decrease in serum triacylglycerol); and

Hunter, JO et al, J. Nutr. 1999 Jul; 129 (7 Suppl): 1451S-3S "Controlled trial of oligofructose in the management of irritable bowel syndrome" (which is understood to compare the effect of Raftilose (2 g three times daily) and of sucrose (1 g three times daily) in patients suffering from irritable bowel syndrome).

The Examiner is requested to confirm consideration of the attached abstracts in his next Action.

The claims are submitted to be patentable over the cited art and withdrawal of the Section 103 rejection of the claims is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably

by telephone, in the event anything further is required to place the application in condition for allowance.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /B. J. Sadoff/
B. J. Sadoff
Reg. No. 36,663

BJS:
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

1: J Nutr. 1999 Jul;129(7 Suppl):1451S-3S.

Controlled trial of oligofructose in the management of irritable bowel syndrome.

Hunter JO, **Tuffnell Q**, **Lee AJ**.

Gastroenterology Research Unit, Addenbrooke's Hospital, Unit 7, Cambridge, England CB2 2QQ, UK.

A double-blind crossover trial of oligofructose (Raftilose P95) 2 g three times daily against sucrose (1 g) three times daily was performed in patients suffering from irritable bowel syndrome. Each treatment was followed for 4 wk. Patients consumed a standardized diet during the last 14 d of each treatment period, and symptoms were assessed using a previously validated questionnaire. Fecal weight and pH, whole-gut transit time and fasting breath hydrogen concentrations were measured at the start of the study and at the end of each treatment period. Oligofructose produced no significant change in any of these parameters even when patients were divided into those with predominant diarrhea (n = 14) and those with predominant constipation (n = 7). Oligofructose at a dose of 6 g/d had no therapeutic value in patients with irritable bowel syndrome.

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1: Br J Nutr. 1996 Dec;76(6):881-90.

Involvement of lipogenesis in the lower VLDL secretion induced by oligofructose in rats.

Kok N, Roberfroid M, Robert A, Delzenne N.

Déparetment des Sciences Pharmaceutiques. Université Catholique de Louvain, Brussels, Belgium.

Dietary supplementation with oligofructose (OFS; 100 g/kg), a non-digestible oligomer of beta-D-fructose, decreases serum triacylglycerols in serum and VLDL of rats. In order to investigate the role of hepatic metabolism in the hypolipidaemic effect of OFS, male Wistar rats were fed on a standard diet with or without 100 g Raftilose P95/kg as OFS source for 30 d. OFS feeding (1) significantly decreased triacylglycerol and phospholipid concentrations in both blood and liver, (2) increased the glycerol-3-phosphate liver content but decreased the hepatic activity of glycerol-3-phosphate acyltransferase (EC 2.3.1.15), suggesting a decrease in acylglycerol synthesis, (3) did not affect the blood non-esterified fatty acid concentrations, but (4) reduced by 54% the capacity of isolated hepatocytes to synthesize and secrete triacylglycerols from labelled acetate; the activity of fatty acid synthase, a key lipogenic enzyme was also significantly decreased. These findings suggest that OFS decreases serum triacylglycerols by reducing de novo fatty acid synthesis in the liver; the lower insulin level in the serum of OFS-fed rats could explain, at least partly, the metabolic effect induced by such non-digestible carbohydrates.

PMID: 9014656 [PubMed - indexed for MEDLINE]